

What is claimed is:

1. A method for identifying one or more genes involved in a response by a cell, tissue or organism to a stimulus, 5 comprising the steps of:

a.) contacting cells, tissues or organisms which are capable of exhibiting a particular response to said stimulus with a library of antisense oligonucleotides prior to treatment with said 10 stimulus; and

b.) determining which antisense oligonucleotides within said library modulate said response, wherein antisense oligonucleotides which modulate said 15 response correspond to gene products involved in said response.

2. The method of claim 1, wherein said cells are divided into one or more substantially identical subpopulations prior to contacting with said library of 20 oligonucleotides, wherein each subpopulation is contacted with one member of said library of antisense oligonucleotides.

3. The method of claim 1, wherein said compound is a cytokine or growth factor.

25 4. The method of claim 3, wherein said cytokine or growth factor is TNF- α , IL-1 or IFN- γ .

5. The method of claim 1, wherein said response is 30 secretion of a compound.

6. The method of claim 5, wherein said compound is a cytokine or growth factor.

5 7. The method of claim 1, wherein said response is modulation of expression of a cell surface protein.

8. The method of claim 7, wherein said cell surface protein is a cell adhesion protein.

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9. The method of claim 1, wherein said response is modulation of inflammation.

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The method of claim 1, wherein said response is

inhibited.

11. The method of claim 1, wherein said response is stimulated.

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12. The method of claim 1, wherein said response is a modulation of apoptosis or cell cycle profile.

13. The method of claim 1, wherein said response is modulation of angiogenesis.

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14. The method of claim 1, wherein said response is modulation of insulin signaling, glycogenolysis or adipocyte differentiation.

15. A method for identifying one or more genes involved in a phenotype of a cell, tissue or organism, comprising the steps of:

5 a.) contacting one or more substantially identical subpopulations of said cell, tissue or organism which exhibits said phenotype with a library of antisense oligonucleotides, wherein each subpopulation is contacted with one member of said library of antisense oligonucleotides; and

10 b.) performing a primary phenotypic assay to determine which antisense oligonucleotides within said library modulate said phenotype, wherein antisense oligonucleotides which modulate said phenotype correspond to genes involved in said phenotype.

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16. The method of claim 15, wherein said phenotype is associated with a disease state.

20 17. The method of claim 15, wherein said disease state is cancer, undesired angiogenesis, inflammation or a metabolic disorder.

25 18. The method of claim 17, wherein said metabolic disorder is diabetes.

19. The method of claim 15, further comprising the step of performing a secondary phenotypic assay.

30 20. The method of claim 19, wherein said secondary phenotypic assay is a low density array.

21. The method of claim 19, further comprising the step of performing a tertiary phenotypic assay.

5 22. The method of claim 21, wherein said tertiary phenotypic assay is a high density array.

10 23. A method for identifying genes expressed in dendritic cells that regulate co-stimulation of T-cells, comprising the steps of:

- a.) culturing dendritic cells in the presence of one or more cytokines to activate said dendritic cells;
- b.) contacting one or more substantially identical subpopulations of said activated dendritic cells with a library of antisense oligonucleotides, wherein each subpopulation is contacted with one member of said library;
- c.) adding T-cells to said antisense oligonucleotide-treated activated dendritic cells; and
- 20 d.) measuring IL-2 production, wherein antisense oligonucleotides which modulate IL-2 production correspond to genes which play a role in co-stimulation of T cells.

25 24. The method of claim 23, wherein said cytokines comprise IL-4 and GM-CSF.

25. The method of claim 23, wherein said antisense oligonucleotide inhibits production of IL-2.

26. A method for identifying genes that play a role in T cell-mediated inflammation, comprising the steps of:

- a.) culturing dendritic cells in the presence of one or more cytokines to activate said dendritic cells;
- 5 b.) contacting one or more substantially identical subpopulations of said activated dendritic cells with a library of antisense oligonucleotides, wherein each subpopulation is contacted with one member of said library;
- 10 c.) adding T-cells to said antisense oligonucleotide-treated activated dendritic cells; and
- d.) measuring IL-2 production, wherein antisense oligonucleotides which inhibit IL-2 production correspond to genes which increase inflammation.

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27. The method of claim 26, wherein said cytokines comprise IL-4 and GM-CSF.

28. The method of claim 26, further comprising the step
20 of adding a CTLA4-Ig fusion protein after treatment with antisense oligonucleotide.

29. A library comprising between about 10 and 10,000 prevalidated antisense oligonucleotides.

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